CLINICO-DIAGNOSTIC PATTERN OF PULMONARY TUBERCULOSIS AMONG HIV PATIENTS

Dissertation submitted for M.D., Degree in General Medicine

Branch -I

The TamilNadu Dr.M.G.R. Medical University

Chennai

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CERTIFICATE

This is to certify that this dissertation titled – CLINICO-DIAGNOSTIC PATTERN OF PULMONARY TUBERCULOSIS AMONG HIV PATIENTS is submitted by DR.S.BALAJI to the TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI, in partial fulfillment of the requirement of the award of M.D. DEGREE BRANCH I (GENERAL MEDICINE) is an original research work carried out by him under our direct supervision and guidance.

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DECLARATION

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This is submitted to the TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY, CHENNAI, in partial fulfillment of the requirement for the award of M.D., degree examination, branch I (General Medicine) to be held on April 2011.

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CLINICO-DIAGNOSTIC PATTERN OF PULMONARY TUBERCULOSIS AMONG HIV PATIENTS

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ABBREVIATIONS

LIST OF ABBREVIATIONS USED IN THE PROFORMA, MASTER CHART AND IN THE DISSERTATION

HIV	HUMAN IMMUNODEFICIENCY VIRUS
PTB/PT	PULMONARY TUBERCULOSIS
ATT	ANTI TUBERCULOUS TREATMENT
ART	ANTI RETROVIRAL THERAPY
HAART	HIGHLY ACTIVE ANTI RETROVIRAL THERAPY
CD4	CLUSTER DIFFERENTIATION 4 CELLS (HELPER T CELLS)
M	MALE
F	FEMALE
MCH	MALE CHILD
FCH	FEMALE CHILD
TC	TOTAL COUNT
DC	DIFFERENTIAL COUNT
ESR	ERYTHROCYTE SEDIMENTATION COUNT
HB	HEMOGLOBIN
SGOT	SERUM GLUTAMIC OXALOACETIC TRANSAMINASE
SGPT	SERUM GLUTAMIC PYRUVIC TRANSAMINASE
ALP	ALKALINE PHOSPHATASE
UZ	UPPER ZONE OF CHEST X RAY
MZ	MIDDLE ZONE OF CHEST X RAY
LZ	LOWER ZONE OF CHEST X RAY
WHO	WORLD HEALTH ORGANISATION
RNTCP	REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME
AZT	ZIDOVUDINE

TDF TINOFOVIR

3TC LAMIVUDINE

FTC EMTRICITABINE

EFV EFAVIRENZ

NVP NEVIRAPINE

NRTI NUCLEOIDE REVERSE TRANSCRIPTASE INHIBITOR

INTRODUCTION

INTRODUCTION

Tuberculosis is a major public health problem in many of the developing countries. This is further complicated by the HIV infection, which is a pandemic disease and also leads to the emergence of the multidrug resistant tuberculosis strains. WHO has declared tuberculosis as a global emergency in 1993 and the member nations adopt various control programmes to control the disease. [1]

HIV infection cause progressive immunodeficiency state, rendering the infected persons to increased susceptibility to various opportunistic infections, as the immune system becomes less able to prevent the growth and spread of the disease. Of these various opportunistic infections Tuberculosis is the most common disease.

Mycobacterium tuberculosis infects one third of the world's population. Worldwide there are about 8 million new cases and 3 million deaths every year. Of the majority of the cases and deaths occur in developing countries.

India has the largest number of tuberculosis (TB) cases in the world. India has 14 million cases of TB and it is estimated that about 1.8 million incident cases of TB occur in India every year. [2]

Individuals infected with M. tuberculosis have an approximately 10% life time risk of developing active TB, whereas the persons infected with HIV have 10% annual risk of getting infected with tuberculosis. Conversely Mycobacterium tuberculosis accelerates the progression of the HIV infection. [3]

Hence it is essential to treat tuberculosis effectively in persons with HIV infection and reducing the mortality of these persons.

OBJECTIVES OF THE STUDY

OBJECTIVES OF THE STUDY

1. To evaluate the clinical, bacteriological and radiological pattern of tuberculosis infection among HIV seropositive individuals in correlation with the CD 4+ counts.

2. To find out the pattern of Tuberculosis infection, in HIV seropositive patients attending Coimbatore medical college hospital.

3. To find the prevalence of Pulmonary Tuberculosis among HIV Seropositive patients attending Coimbatore Medical College hospital.

4. To find the correlation between the manifestations of pulmonary tuberculosis and the CD4 count at the time of diagnosis of pulmonary tuberculosis.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

TUBERCULOSIS

is an ancient disease caused by the organism Mycobacterium tuberculosis .It was first discovered by Robert Koch in 1882. It is slightly curved or straight bacilli of size 0.2 to 0.6 by 1.0 to 10 microns. [4] Tuberculosis is also caused by Mycobacterium bovis and Mycobacterium africanum occasionally. These bacteria are also known as tubercle bacilli or acid fast bacilli (AFB). [5]

M. tuberculosis infects a third of the world's population. In 2000 there were an estimated 8.3 million new cases of TB worldwide. 95% of TB cases and 98% of TB deaths are in developing countries. 75% of TB cases in developing countries are in the economically productive age group (15–50 years).There was 1.8 million deaths from TB in 2000, with 2, 26,000 cases attributable to HIV (12%).TB deaths comprise 25% of all avoidable adult deaths in developing countries. India alone is estimated to have 5.1 million PLWH. Every year, 1.8 million TB cases are notified and treated under DOTS in India. Between 2.5 to 3 million people in the Region are currently estimated to be infected with both HIV and TB [6].

The bacterium has high lipid content in the cell wall which includes mycolic acid, which is not readily stained with Gram stain. Hence special staining techniques are required to promote the uptake of the stain. Hence acid-fast detection techniques are used. The bacterium is detected by Ziehl-Neelsen staining method or by Fluochrome staining methods using auramine or auramine-rhodamine fluorescein stains. The bacteria grow well in Lowenstein- Jensen medium with incubation period of two to five weeks.

Mycobacterium tuberculosis is an obligate aerobe. For this reason, in the classic case of tuberculosis, MTB complexes are always found in the well-aerated upper lobes of the lungs. The bacterium is a facultative intracellular parasite, usually of macrophages, and has a slow generation time, 15-20 hours, a physiological characteristic that may contribute to its virulence.

The Tuberculosis genome was sequenced in 1998. Its size is 4 million base pairs, with 3959 genes. The genome contains 250 genes involved in fatty acid metabolism, with 39 of these involved in the polyketide metabolism generating the waxy coat. Such large numbers of conserved genes shows the evolutionary importance of the waxy coat to pathogen survival.

SOURCE OF INFECTION:

The most important source of infection is the tiny infectious droplet nuclei coughed out by the infected patient. A single cough can produce 3000 droplet nuclei. Droplet nuclei also spread by talking, sneezing, spitting and singing, and can remain suspended in the air for long periods. Direct sunlight kills the tubercle bacilli in 5 minutes, but they can survive in the dark for long periods. Transmission therefore generally occurs indoors. Droplet nuclei are so small that they avoid the defense of the bronchi and penetrate into the terminal alveoli of the lungs, where multiplication and infection begin. Two factors determine an individual's risk of exposure: the concentration of droplet nuclei in contaminated air and the length of time he or she breathes that air. The infected persons develop the disease at any time. The disease affects almost all organs of the body, lung being the most commonly affected. The most important trigger for the progression from infection to disease is the weakening of the immune resistance as in HIV infection. If untreated 50% patients die, 25% live healthy and 25 % will remain ill with chronic infectious TB.

PATHOGENESIS

Primary infection:

This occurs in persons not exposed to the bacilli previously. Here the bacilli are deposited in the terminal bronchiole and the alveoli, wherein they develop the Ghons focus, with lymphatic spread develop the Ghons complex. Then the infection might spread to all over the body later. Here the immunity develops in

4 to 6 weeks period (delayed hypersensitivity and cellular immunity). In most cases due to this immunity the bacilli either stops multiplying or may remain as dormant bacilli the body itself.

Post primary infection:

This occurs after months to years after the primary infection. Here there is either reactivation of the dormant bacilli or reinfection.

The CD4 cells which are MHC class II restricted CD4 lymphocytes, play a key role in the immune response against tuberculosis, as they produce IFN gamma and activating cytokines which are necessary to contain the infection.

CLINICAL FEATURES OF TUBERCULOSIS [7]

Primary infection:

May cause

1. No clinical disease.

2. Positive tuberculin test.

3. Hypersensitivity reactions like erythema nodosum, phylecten etc.

4. Pulmonary/ pleural - pneumonia , consolidation, collapse, effusion.

5. disseminated disease like military TB, meningitis, pericarditis, lymphadenopathy.

Post primary infection:

May cause

1. Pulmonary TB as cavities, infiltrates, progressive pneumonia, endobronchial TB.

2. Extrapulmonary as pleural effusion, lymphadenopathy , meningitis, tuberculoma, GI TB, genital tract TB, renal , adrenal TB and skin manifestations .

Clinical symptoms needed for the diagnosis of the Pulmonary tuberculosis are:

Cough for more than 3 weeks,

Sputum production,

Weight loss.

Other symptoms are chest pain, hemoptysis and dyspnoea, along with constitutional symptoms of fever, night sweats, tiredness, loss of apetitite etc.

Physical signs are not disease specific for tuberculosis. They do not help to differentiate from other respiratory infections.

INVESTIGATIONS

SPUTUM AFB: Two samples of early morning sputum for Zeihl – neelson staining.

Chest radiograph to diagnose the sputum negative cases may show classically infiltrations in upper zones, cavities in upper zones and atypically the interstitial infiltration, lymphadenopathy, pleural effusion etc.

CULTURE OF THE M. tuberculosis [8] done using LJ medium. This is gold standard test for the diagnosis of Tuberculosis. But it takes more than 8 weeks for the bacilli to be cultured and needs culture facility and laboratory skills. Hence not readily available and cannot be done regularly.

Other methods are

BACTEC 460 TB system

ESP Culture II System

BacT/Alert MB

MGIT tube system

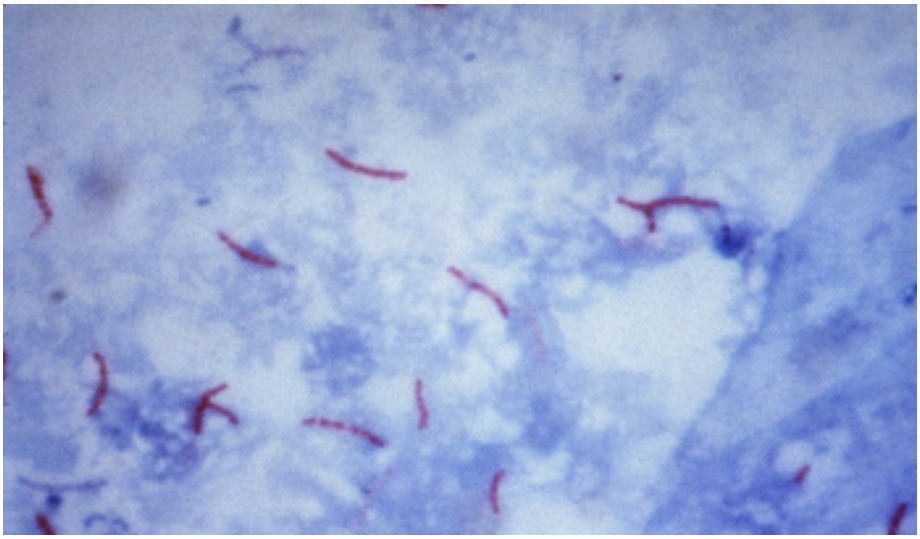
Chromatographic identification

Identification by nucleic acid probes

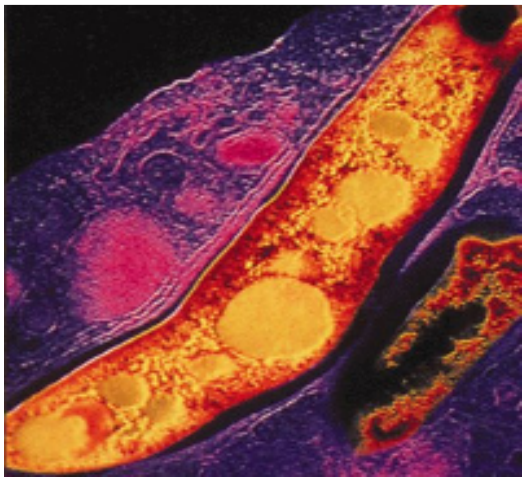
Molecular methods like AMTD test, Roche

Amplicor M.TB test based on PCR assay.

MYCOBACTERIUM TUBERCULOSIS – OIL IMMERSION VIEW



MYCOBACTERIUM TUBERCULOSIS - ELECTRON MICROSCOPIC VIEW



HUMAN IMMUNODEFICIENCY VIRUS

First discovered by Luc Montaineger in 1983, named as LAV 2, simultaneously Robert Gallo discovered in 1984, named as HTLV III. Both were later found to be the same virus, hence was redesignated as HIV by the International Committee on taxonomy of viruses. A variant of this HIV was identified at western Africa, hence the former was known as HIV 1 and the latter as HIV 2. A similar virus is reported in African green monkeys, named SIV (Simian Immunideficiency Virus) [9].

HIV virus belongs to the class Retroviruses and family Lentivirinae. It has an outer envelope of lipid bilayer with uniformly arranged 72 spikes or knobs gp120 and gp 41. It has a single stranded RNA virus in its core along with enzymes reverse transcriptase, integrase and protease, all needed for viral replication and maturation. Surrounding this is P17 core Gag protein, which is needed to maintain the integrity of the viral particle. The size of the genome is 9 kb.

As the virus enters the blood stream, it binds to CD4 receptor on the T lymphocyte via the gp 120 cover, enters the cell

cytoplasm, uncoats its envelope, and sheds the viral RNA and the enzyme reverse transcriptase.

This enzyme facilitates conversion of viral RNA to DNA-pro viral DNA. This then creates its mirror image using the enzyme integrase. This then unites with the host genome becomes its integral part. It multiplies repeatedly, produces m RNA along with multiplication of the host nucleus. The mRNA directs the host cells to produce the new viral particles with the help of the enzyme protease. This small virions bud out of the host cell to infect another host cell. During the active replication stage around one billion viruses are produced daily.

HIV virus is very fragile. It is inactivated at temp of 56C for 30 mins or boiling for few seconds. Also inactivated by 0.2%sodium hypochlorite, 2%glutaraldehyde, 70%ethanol, betapropiolactone etc.

The virus is transmitted by sexual intercourse, blood transfusion, perinatal transmission, IV drug abuse – sharing of infected needles, needle stick injuries etc.

HIV virus cause progressive impairment of cellular immune response, decline in the CD4 count increased susceptibility to opportunistic infections and certain malignancies also. The disease progresses as

1. Typical progressors with mean survival time of 10 years,
2. Rapid progressors with mean survival time of 3-4 years and

3. Long term non progressors who do not experience the HIV disease.

Revised World Health Organization (WHO) Clinical Staging of HIV/AIDS for Adults and Adolescents (2005)

Primary HIV infection

- Asymptomatic
- Acute retroviral syndrome

Clinical stage 1

- Asymptomatic
- **Persistent generalized lymphadenopathy**

Clinical stage 2

- Moderate and unexplained weight loss (<10% of presumed or measured body weight)
- Recurrent respiratory tract infections (such as sinusitis, bronchitis, otitis media, pharyngitis)
- Herpes zoster
- Recurrent oral ulcerations
- Papular pruritic eruptions
- Angular cheilitis
- Seborrhoeic dermatitis
- Fungal finger nail infections

Clinical stage 3

Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations

- Unexplained chronic diarrhea for longer than one month
- Unexplained persistent fever (intermittent or constant for longer than one month)
- Severe weight loss (>10% of presumed or measured body weight)
- Oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis (TB) diagnosed in last two years
- Severe presumed bacterial infections (e.g. pneumonia, empyema, meningitis, bacteraemia, pyomyositis, bone or joint infection)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis

Conditions where confirmatory diagnostic testing is necessary

- Unexplained anaemia (< 80 g/l), and or neutropenia (<500/µl) and or thrombocytopenia (<50 000/ µl) for more than one month

Clinical stage 4

Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe or radiological bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration)
- Oesophageal candidiasis
- Extrapulmonary Tuberculosis
- Kaposi's sarcoma
- Central nervous system toxoplasmosis
- HIV encephalopathy

Conditions where confirmatory diagnostic testing is necessary

- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacteria infection
- Progressive multifocal leukoencephalopathy
- Candida of trachea, bronchi or lungs
- Cryptosporidiosis

- Isosporiasis
- Visceral herpes simplex infection
- Cytomegalovirus (CMV) infection (retinitis or of an organ other than liver, spleen or lymph nodes)
- Any disseminated mycosis (e.g. histoplasmosis, coccidiomycosis, penicilliosis)
- Recurrent non-typhoidal salmonella septicaemia
- Lymphoma (cerebral or B cell non-Hodgkin)
- Invasive cervical carcinoma
- Visceral leishmaniasis

DIAGNOSIS

Is by

1. EIA - enzyme immune assay, good screening test, sessitivity > 99.5%

2. Western blot – mostly commonly used confirmatory test.

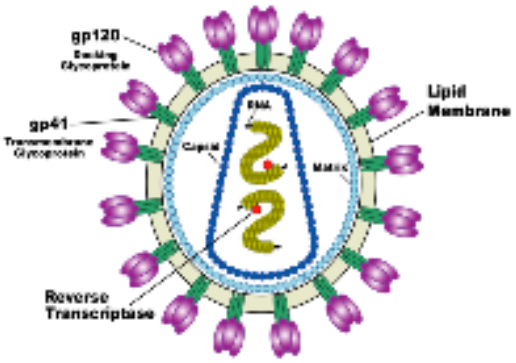
3. Direct detection test – p 24 antigen capture assay.

4. RT PCR-to detect the HIV RNA.

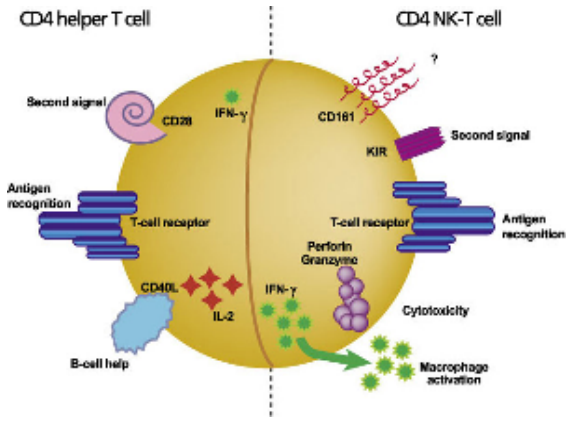
MONITORING of the patients' infection is by CD4 count It is the best indicator of the immediate state of immunologic competence of the patient. If < 350 anti retroviral therapy (ART) to be initiated, if < 200, PCP prophylaxis to be started, if < 50. Prophylaxis against MAC to be started.

Other means are by HIV RNA measurement in the serum or plasma. [10].

HIV VIRUS – A DIAGRAMATIC REPRESENTATION



CD 4 CELL A DIAGRAMATIC REPESENTATION



HIV RELATED TB

By the end of 2000, 11.5 million HIV infected people were coinfected with M .tuberculosis worldwide. 70% were in sub Saharan Africa, 20% in South East Asia and 4% in Latin America and Caribbean [(11)]according to WHO, 39% of the Tuberculosis cases are seen in South East Asia, of these, 95 % cases are reported from India, Indonesia, Myanmar and Thailand.[(12).]

Tuberculosis has a lifetime risk of infection of 10% in non HIV population, whereas in HIV infected it carries a annual risk of 10% every year, which means HIV patients have 10 times the risk of developing the TB than the non HIV patients. This is by means of either reactivation of the latent TB infection by immunosuppression or by reinfection with MTB. HIV does not enhance the infectiousness of the individual patients with TB.

Conversely MTB induces progression of the HIV immunosuppression by inducing the replication if HIV in cells of the monocyte lineage by TNF alpha and various chemokines and by activation of latent HIV in alveolar macrophages or in monocytes. The viral load increases by 2.5 fold at the diagnosis of TB. This may also explain the low CD4 count in the HIV patients who are on HAAT

diagnosed to have tuberculous infection during their course of treatment for HIV disease. Thus there is a complex immunological interaction of HIV and TB infection [13] leading to progression of both the infections.

The pattern of the HIV related TB is that , due to immunosuppression , the immune system is unable to prevent the growth and local spread of the tuberculosis; hence more immunosuppression, more the disseminated and extrapulmonary TB. Even in HIV infected persons pulmonary tuberculosis is the most common presentation. But its presentation varies with the disease activity.

In early HIV disease, the clinical picture resembles post primary PTB, sputum AFB is often positive and X ray shows cavities. Whereas in late HIV disease, the clinical picture resembles that of primary PTB, sputum AFB is often negative, and X ray shows often infiltrates rather than cavities. [14]

In HIV-infected patients with pulmonary TB, cultures are positive in about 90% of cases and sputum smears are positive in about 50% to 70%--numbers that are similar to those seen in immunocompetent adults with reactivation TB [15].

Latent Tuberculosis Infection (LTBI)

Screening for latent tuberculosis infection (LTBI) is an essential step in controlling the spread of tuberculosis. Screening for LTBI is recommended in persons at risk for recent infection and in those groups with increased risk of progression to active disease once infected, including HIV-infected persons. The tuberculin skin test using 1 TU (Tuberculin unit) – Mantoux test, is currently the only method available for identifying LTBI. Routine annual tuberculin skin testing is recommended in HIV-infected individuals.

A reaction of >5 mm induration is considered positive for HIV-infected patients and persons with other forms of severe immunosuppression, persons who are close contacts of infectious cases, and persons with abnormal chest radiographs consistent with tuberculosis[16]. Use of the 5-mm cutoff is supported by a prospective study in the United States demonstrating that the risk of tuberculosis was significantly higher in HIV-infected persons with tuberculin skin test reactions >5 mm of induration than in those who have a reaction <5 mm.[17].

It is important to keep in mind that a negative tuberculin skin test does not exclude infection or active disease. Testing with tuberculin purified protein derivative is dependent on the presence of an intact cell-

mediated immune response. In the setting of HIV infection, reduced cell-mediated immunity can lead to decreased delayed-type hypersensitivity (DTH) responsiveness, resulting in False-negative skin tests. In a multicenter study in the United States, the prevalence of a positive tuberculin skin test (>5 mm) was shown to decrease with decreasing CD4 T-cell counts. [18]

The Threat of Drug Resistance

If a TB drug regimen is not completed or is taken sporadically, TB bacteria can develop resistance to the drugs, so the drugs are no longer effective at killing the bacteria. People with HIV/AIDS are at even greater risk for developing drug-resistance because they may not absorb the medicines as well as others. Also, because their immune system is damaged, it is unable to help the TB medicines get rid of the TB bacteria. The threat of active tuberculosis, including drug resistant TB, continues for HIV patients, even after they are successfully managed on HIV antiretroviral therapy.

Multidrug-resistant TB (MDR TB) can develop when bacteria become resistant to the two most powerful first line drugs (isoniazid and rifampicin). When this happens, second-line drugs are required, which are more expensive and have more side effects.

Extensively drug-resistant TB (XDR TB) can develop when second-line therapies are not used properly and the, bacteria develop resistance to them as well. Treatment options are extremely limited for people with XDR TB and the risk of death is extremely high—particularly for people living with HIV/TB. [19]

TREATMENT OF TUBERCULOSIS AND HIV DISEASE

TREATMENT OF TUBERCULOSIS

Category of Treatment	Type of patient	Regimen	Sputum Examination
CAT-I	New sputum smear positive/ negative Seriously ill / not seriously ill sputum-negative Seriously –ill/ not seriously ill EP	2 H3R3Z3E3/ 4 H3R3	0 2 4 6 3 5 7 MONTHS
CAT- II	Sputum smear + Relapse, Failure, Treatment after Default	3 H3R3Z3E3S3/ 1 H3R3Z3E3/ 5 H3R3E3.	0 3 5 8 4 6 9

In the latest RNTCP guidelines 2010, the Category III has been removed; instead the cases are treated with Category I.

WHO recommendations for the treatment of TB and HIV co infection

with reference to CD-4 cell count.

CD 4 cell count	Recommended regimen	Comments
< 200 mm^3	Start TB treatment. Start ART as soon as TB treatment is tolerated (2 weeks to 2 months) EFV containing regimens.	Recommended ART EFV is contraindicated in pregnant or women of childbearing potential without effective contraception
200 to 350 mm^3	Start TB treatment. start one of the below regimens after initiation phase: EFV containing regimens or NVP containing regimens in case of Rifampicin free continuation phase TB treatment regimen.	Consider ART
> 350 mm^3	Start TB treatment.	Defer ART
CD 4 count not available	Start TB treatment.	Consider ART

The WHO recommended treatment regimen - 2010 for HIV and PTB co-infection is

AZT or TDF + 3TC (zidovudine +tinofovir+ lamivudine) or

FTC + EFV (emtricitabine+ efavirenz)

Initiate ART as soon as possible (within the first 8 weeks) after starting TB treatment.

NVP or triple NRTIs are acceptable options if EFV cannot be used(nvp – nivirapine)

Abbreviations:

. AZT- zidovudine, TDF- tinofovir,

3TC- lamivudine, FTC- emtricitabine ,

EFV- efavirenz, NVP- nevirapine,

NRTI- nucleoide reverse transcriptase inhibitor.

PARADOXICAL REACTION

Is defined as a temporary exacerbation of symptoms, signs and radiological manifestations of TB after days to weeks of ATT. This is seen in patients with TB adenitis without HIV infection. And it is seen more so in HIV infected persons that too more in those on HAART. The immune reconstitution response is the likely explanation for this. It is generally self limiting in 10 to 14 days, rarely if the reaction is very severe, then HAART may be stopped temporarily and corticosteroids may be started. [20, 21]

MATERIALS AND METHODS

MATERIALS AND METHODS

Methodology

This study was conducted from March 2010 to October 2010, at Coimbatore Medical College Hospital, Coimbatore.

Two sets of patients were selected for the study.

1. Patients attending the OP departments of Medicine and Thoracic Medicine or patients who were admitted at the Medical wards with symptoms suggestive of Pulmonary tuberculosis, (cough of more than three weeks duration, fever, hemoptysis, loss of weight etc) were screened for Pulmonary Tuberculosis with Chest X Ray investigation and Two samples of Sputum AFB. If these patients were found positive for pulmonary tuberculosis, they were screened for HIV disease at the ICTC centre. [22] If found positive, they were included in the study with the consent of the patient.

   Screening for HIV disease was done by the ELISA Rapid

   diagnostic tests

   a. Combiaids
   b. Instachek
   c. Acon Biotech.

If one test was positive, the remaining other two tests were performed and if found positive, the diagnosis of HIV was made as per the guidelines.

2. HIV positive patients who were either under observation or under HAART, who developed symptoms and signs suggestive of Pulmonary Tuberculosis were screened for the same; if found positive for Pulmonary tuberculosis , they were included in the study after obtaining their consent.

   These patients were investigated as following:

   a. Chest X - Ray PA view, if needed Lateral view (if not done earlier).
   b. Sputum for AFB two early morning samples (if not done earlier).
   c. Blood hemoglobin, total count differential count, Erythrocyte sedimentation rate, sugar, urea
   d. Serum creatinine, Liver function test.
   e. CD4 count

   The chest X -ray was taken by digital imaging, read by a general physician, chest physician and a radiologist to diagnose pulmonary tuberculosis.

   The blood investigations were done by conventional methods.

   Sputum AFB was done by ZIEHL NEELSON method.

CD4 count was done by the PARTEC CYFLOW COUNTER (flow cytometer).

INCLUSION CRITERIA:

Patients with symptoms of pulmonary tuberculosis, who were confirmed with the diagnosis of Pulmonary tuberculosis - both Sputum AFB positive and Sputum AFB negative (diagnosed radiologically).

Patients with Tuberculous Pleural Effusion were included in the study.

EXCLUSION CRITERIA:

1. Patients who were suffering from Extra-pulmonary Tuberculosis infections like TB Pericarditis, TB meningitis, TB Abdomen, isolated TB lymphadenopathy, Potts Spine and other seriously ill patients.
2. Patients found to have positivity in only one of the three ELISA tests for HIV.
3. No consensus among all the three independent observers regarding the X-Ray features of Pulmonary Tuberculosis.
4. Patients suspected or confirmed Latent Tuberculosis Infection(LTBI).

STUDY LIMITATIONS:

The confirmation of HIV infection could not be done by Western Blot analysis.

The sputum positivity for tuberculosis could not be confirmed by AFB culture as the procedure was expensive, needed technical experience and also was not available at this hospital.

OBSERVATIONS AND RESULTS

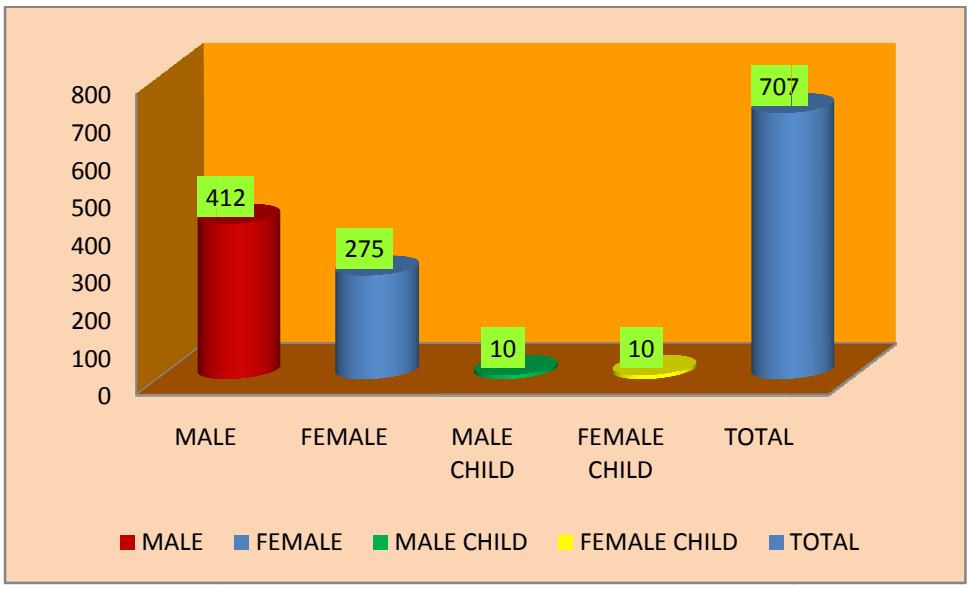
OBSERVATIONS AND RESULTS

The study was done during a period from March 2010 to October 2010 at Coimbatore Medical College Hospital, out of 707 HIV positive patients, 59 cases were diagnosed as pulmonary tuberculosis which included pleural effusion also.

Number of HIV positive cases observed from

March 2010 to October 2010

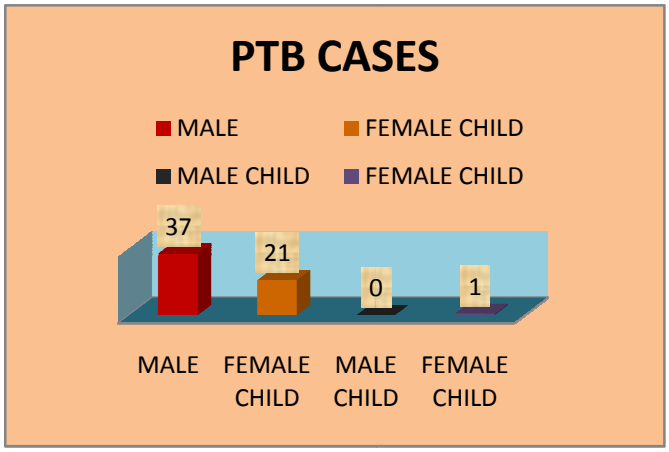
MALE	FEMALE	MALE CHILD	FEMALE CHILD	TOTAL
412	**275**	**10**	**10**	**707**

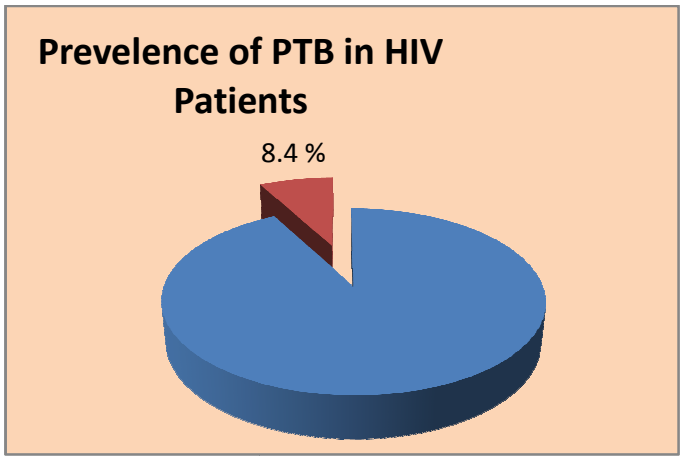


Out of the707 HIV positive cases, 59 were diagnosed as pulmonary tuberculosis including pleural effusion.

Of the 59 cases

Male cases	**38**	63%
Female cases	**20**	36%
Male child	**0**	0
Female child	**1**	1%
Total	**59**	

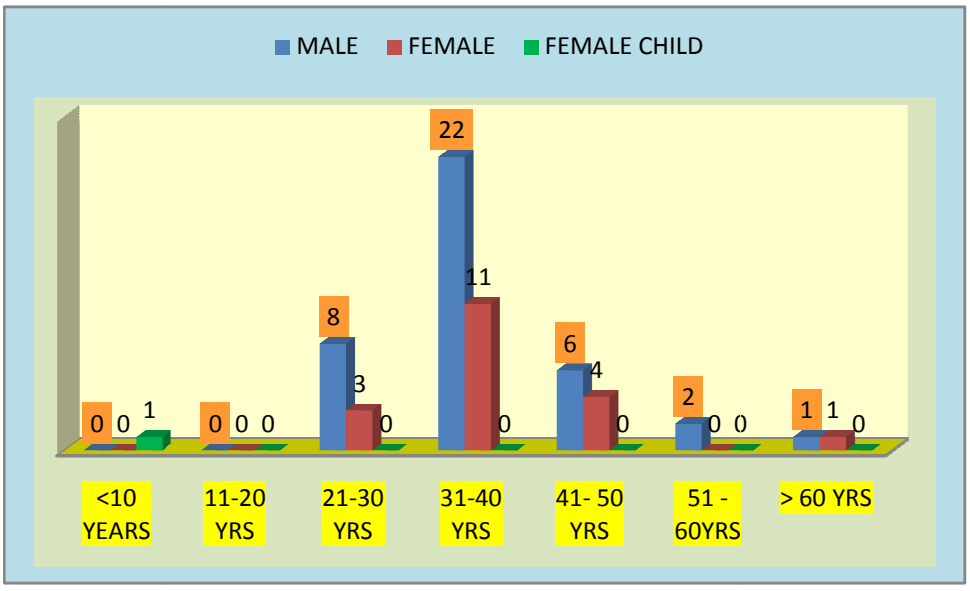




The prevalence of pulmonary tuberculosis in the HIV positive cases was 8.4%. (59 out of 707 cases)

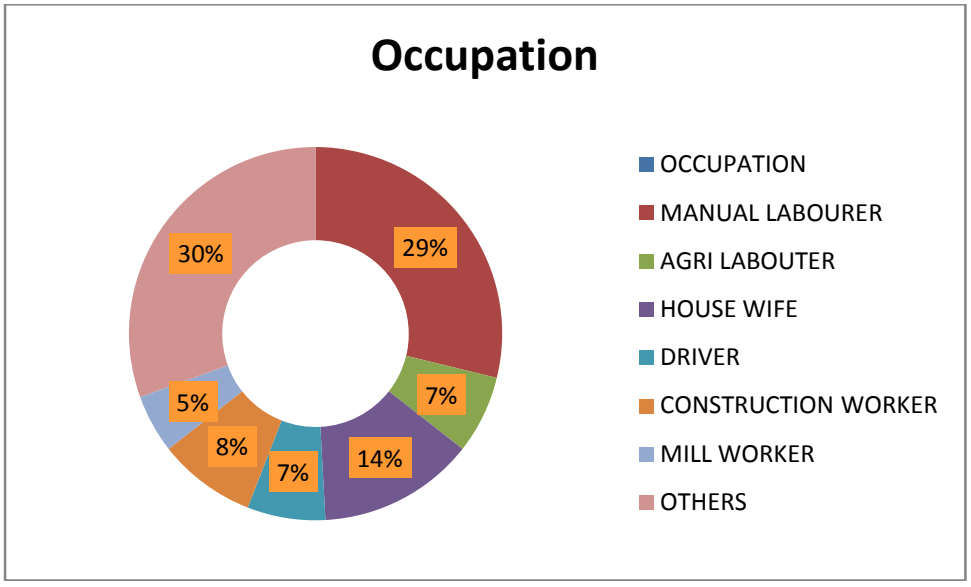
The age **wise distribution** of the cases was as follows:

AGE	MALE	%	FEMALE	%	MALE CHILD	%	FEMALE CHILD	%
< 10 YEARS	0	0	0	0	0	0	**1**	1.6%
11 TO 20 YEARS	0	0	0	0	0	0	0	0
21 TO 30 YEARS	**8**	13.6%	**3**	5.2%	0	0	0	0
31 TO 40 YEARS	**22**	37.4%	**11**	18.6%	0	0	0	0
41 TO 50 YEARS	**6**	10.3	**4**	6.8%	0	0	0	0
51 TO 60 YEARS	**2**	3.3%	0	0	0	0	0	0
>60 YEARS	**1**	1.6%	**1**	1.5%	0	0	0	0



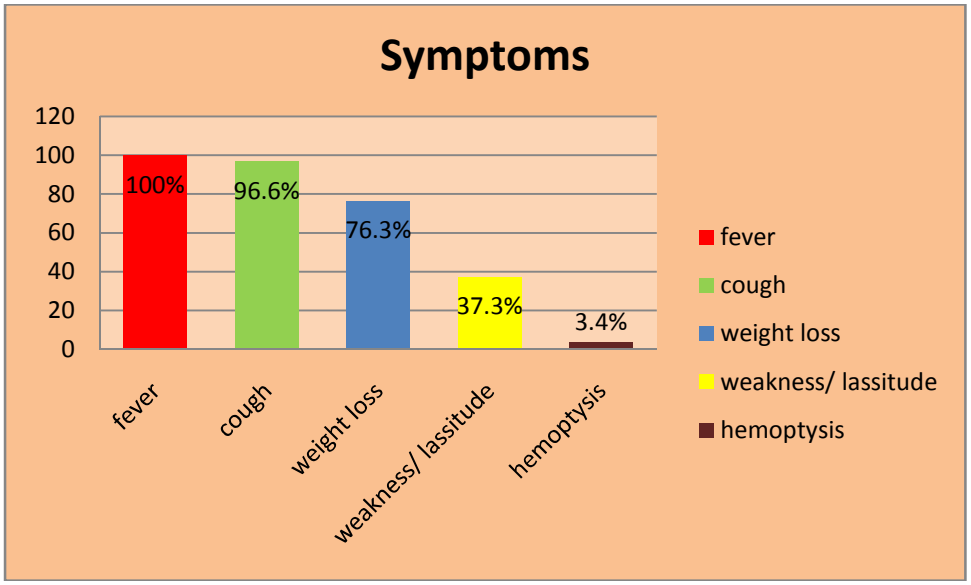
The **occupation** of these patients were as follows:

Manual labourer	17	29%
Agricultural labourer	4	7%
House wife	8	14%
Driver	4	7%
Mill worker	3	5%
Construction worker	5	8%
Others like students, dhobi, sales man, business, veg. vendor, etc.	18	30%



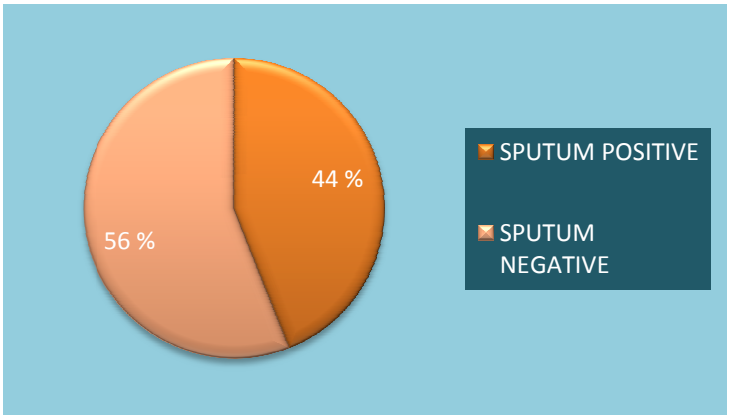
These patients presented with the following SYMPTOMS predominantly.

SYMPTOMS	CASES IN NUMBER	PERCENTAGE
Fever	59	100%
Cough	57	96.6%
Weight loss	45	76.3%
Weakness/ lassitude	22	37.3%
Hemoptysis	2	3.4%



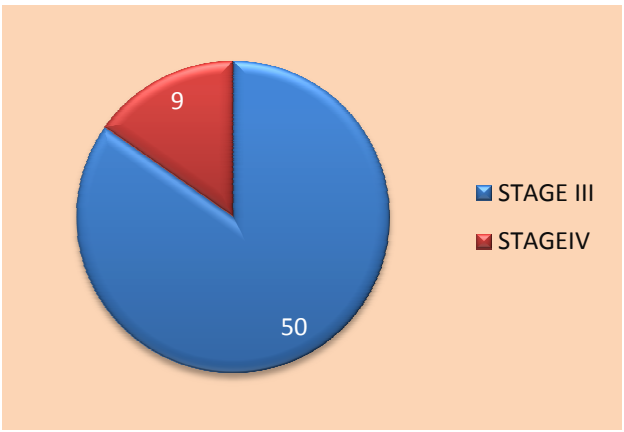
The **Sputum AFB** results were as follows:
Total no. of cases : 59

SPUTUM AFB	CASES	%
POSITIVE	**26**	**44**
NEGATIVE	**33**	**56**



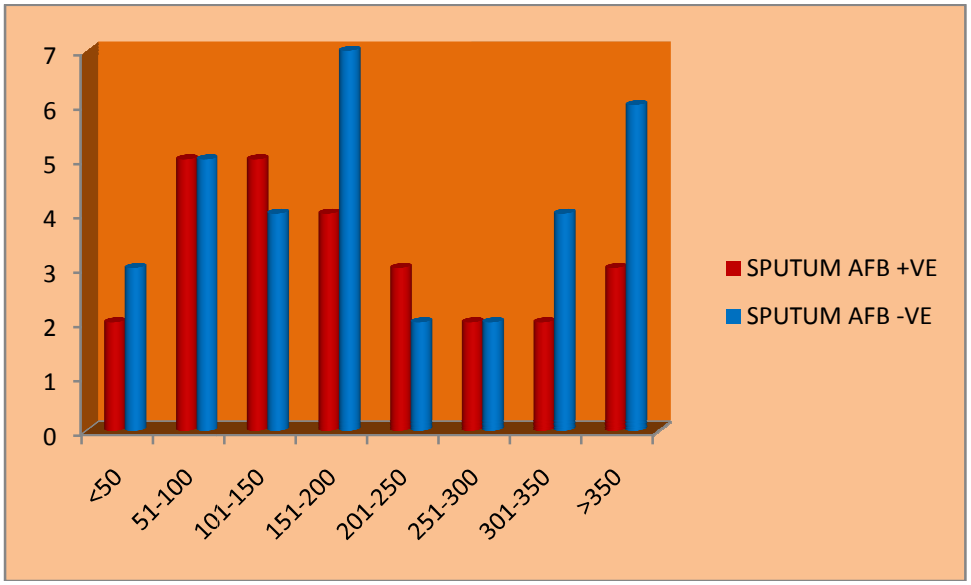
The **WHO staging** of these 59 cases were

STAGE III	50
STAGE IV	9



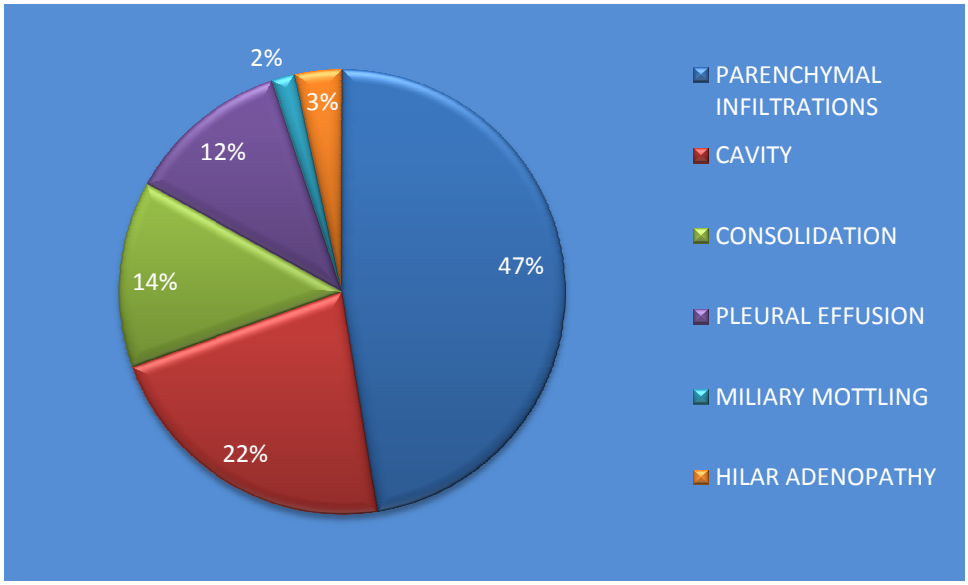
The Sputum AFB status in correlation to the CD4 count was as follows:

CD 4 COUNT	SPUTUM AFB POSITIVE	SPUTUM AFB NEGATIVE
<50	2	3
50-100	5	5
101-150	5	4
151-200	4	7
201-250	3	2
251-300	2	2
301-350	2	4
>350	3	6



The **CHEST X - RAY FINDINGS** in the patients of HIV/ PTB were as follows:

CHEST X RAY FINDINGS	NO. OF CASES	%
PARENCHYMAL INFILTRATIONS	28	47%
CAVITY	13	22%
CONSOLIDATION	8	14%
PLEURAL EFFUSION	7	12%
MILIARY MOTTLING	1	2%
HILAR ADENOPATHY	2	3%

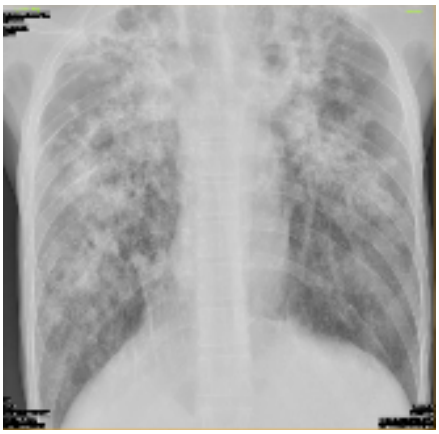


RIGHT UPPER LOBE INFILTRATION

RIGHT UPPE LOBE CONSILODATION

CAVITY LEFT UPPER LOBE

RIGHT PLEURAL EFFUSION

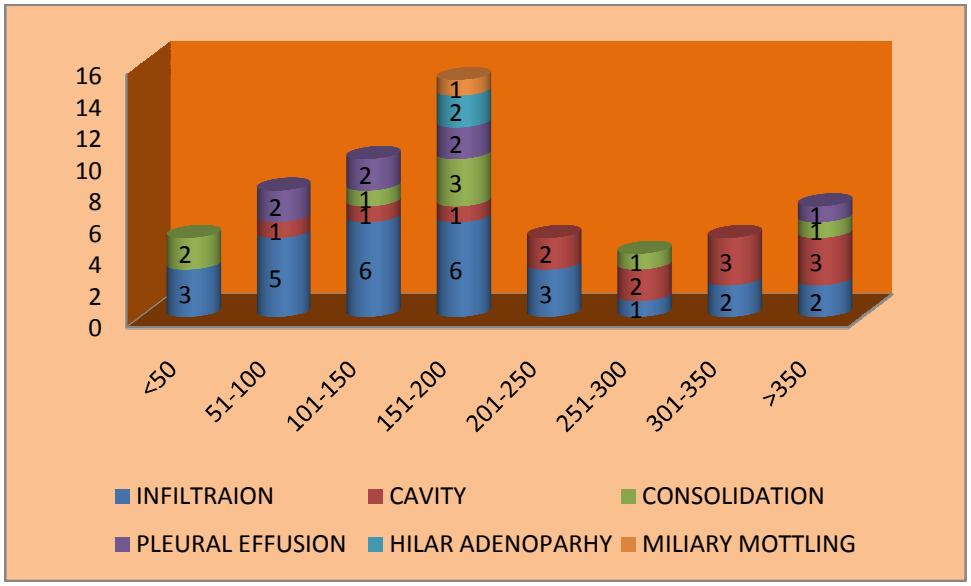


MILIARY TUBERCULOSIS

BILATERAL PULMONARY TUBRCULOSIS

THE CHEST X RAY FINDINGS IN CORRELATION WITH CD4 COUNT

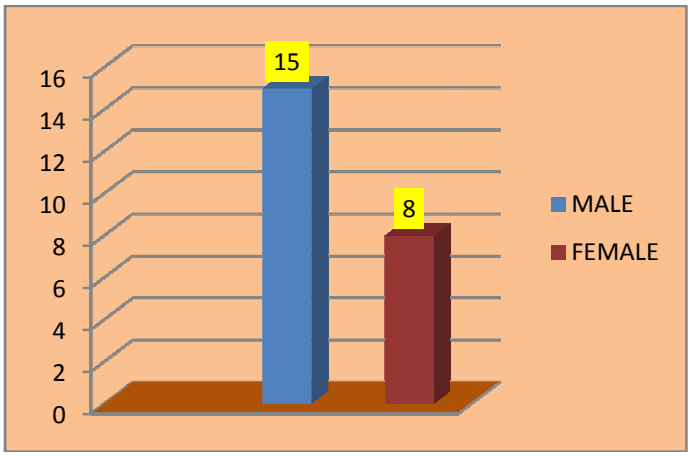
CD4 COUNT	Infiltration	%	cavity	%	consolidation	%	Pleural effusion	%	Hilar adenopathy	%	Miliary mottling	%
<50	3	5	-	-	2	3.3	-	-	-	-	-	-
50-100	5	8	1	1.6	-	-	2	3.3	-	-	-	-
101-150	6	10	1	1.6	1	1.6	2	3.3	-	-	-	-
151-200	6	10	1	1.6	3	5	2	3.3	2	3.3	1	1.6
201-250	3	5	2	3.3	-	-	-	-	-	-	-	-
251-300	1	1.6	2	3.3	1	1.6	-	-	-	-	-	-
301-350	2	3.3	3	5	-	-	-	=	-	-	-	-
>350	2	3.3	3	5	1	1.6	1	1.6	-	-	-	-



Of the 59 cases, 23 cases were on **HAART** prior to diagnosis of PTB

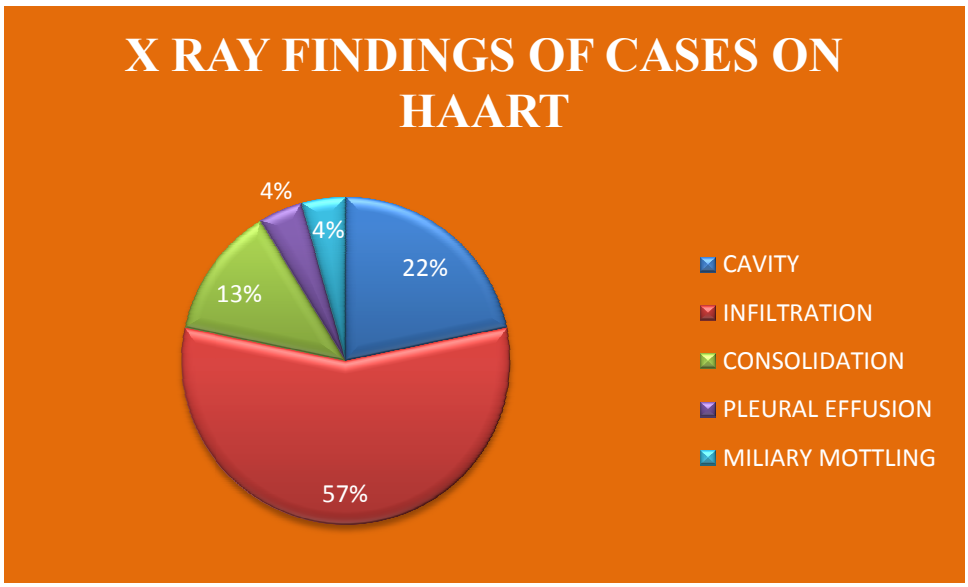
TOTAL NO. OF CASES ON HAART = 23

Male	15
Female	8



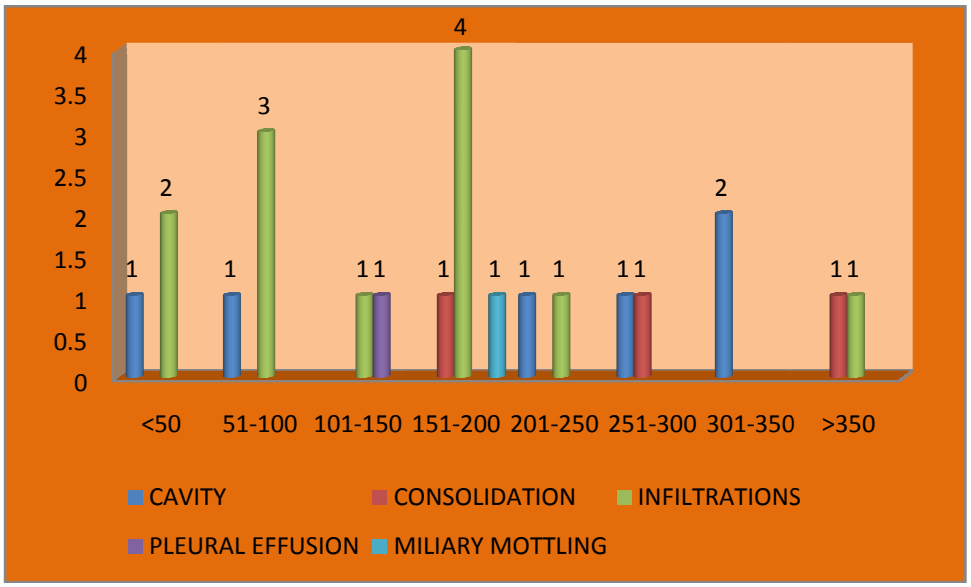
CHEST X RAY FINDINGS IN HIV POSITIVE PATIENTS ON HAART WHO DEVELOPED PTB

X RAY FINDINGS	NO. OF CASES	%
CAVITY	5	22
INFILTRATION	13	57
CONSOLIDATION	3	13
PLEURAL EFFUSION	1	4
MILIARY MOTTLING	1	4



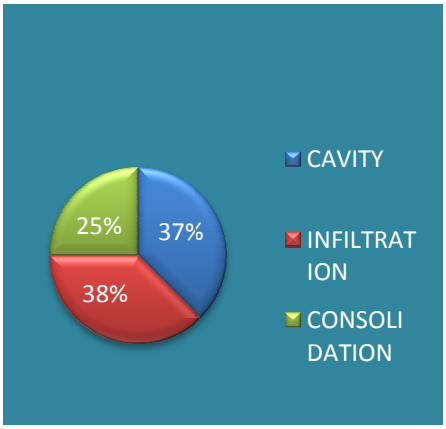
CHEST X RAY FINDINGS IN CORRELATION TO CD4 COUNT IN PATIENTS ON HAART WHO DEVELOPED PTB LATER

CD4 COUNT	CAVITY	%	CONSOLIDATION	%	INFILTRATION	%	PLEURL EFFUSION	%	MILIARY MOTTLING	%
<50	1	4.3	-	-	2	8.7	-	-	-	-
51-100	1	-	-	-	3	13	-	-	-	-
101-150	-	-	-	-	1	4.3	1	4.3	-	-
151-200	-	-	1	4.3	4	17.3	-	-	1	4.3
201-250	1	4.3	-	-	1	4.3	-	-	-	-
251-300	1	4.3	1	4.3	-	-	-	-	-	-
301-350	2	8.7	-	-	-	-	-	-	-	-
>350	-	-	1	4.3	1	4.3	-	-	-	-

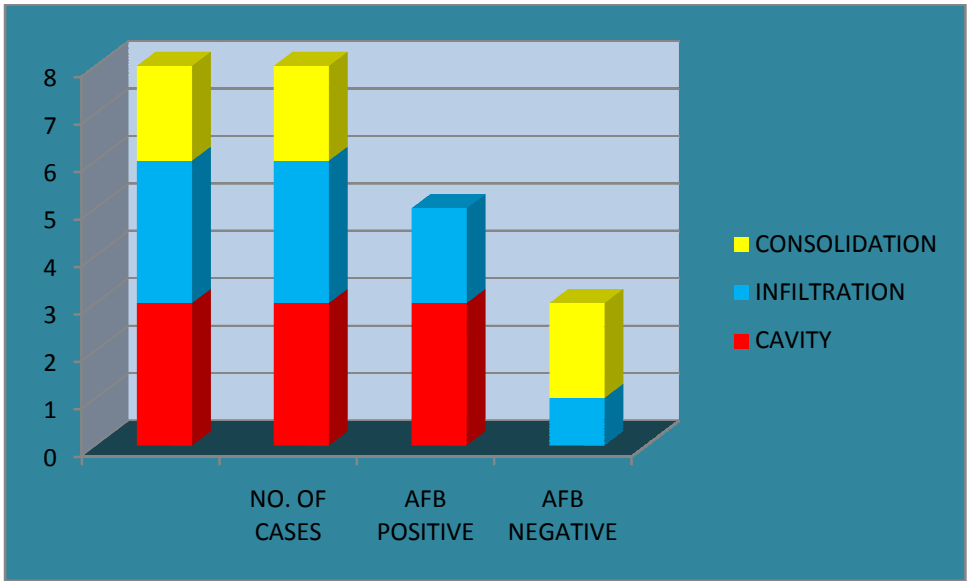


X RAY AND SPUTUM AFB STATUS IN PATIENTS TREATED WITH CAT II ATT IN HIV POSITIVE CASES

X RAY FINDINGS	NO. OF CASES	PERCENTAGE
CAVITY	3	37 %
INFILTRATION	2	38 %
CONSOLIDATION	3	25 %
TOTAL	8	



X RAY FINDINGS	NO. OF CASES	SPUTUM AFB POSITIVE	SPUTUM AFB NEGATIVE
CAVITY	3	3	-
INFILTRATION	3	2	1
CONSOLIDATION	2	-	2



DISCUSSION

DISCUSSION

The study conducted showed out of 707 cases of HIV disease, 59 cases were found to have been suffering from pulmonary tuberculosis, ie 8.4% of HIV positive cases. This is in support of the study conducted by Neeraj Raizada et al in 2008 which showed a prevalence varying between 1& to 13.8 % in various states of India. [24] The observation also correlates with the study conducted by N. Kumarasamy et al. in 2005, which showed prevalence of HIV among patients with radiologic or bacteriologic confirmation of TB in India ranges from 2.8 to 9.4 per cent.[25]

The study conducted out of 59 cases 63% were male, 36% were female and 1% was female child, showing a increased prevalence of HIV/PTB smong male population. This study correlated with the study of HIV seroprevalence was higher among male tuberculosis patients than female tuberculosis patients by Neeraj Raizada et al in 2008. [25]

From the study conducted, it was observed that the age groups between 21 to 40 years were commonly affected from HIV and PTB ie.75%. This observation correlated with the study conducted by C.N. Deivanayagam et al. - 74.1%. [26]

The average age affected by the disease was 37.1, which indicates that, the economically productive group of the population is at the greatest risk of tuberculosis HIV co-infection, thereby causing a heavy socioeconomic loss by and large.

With regard to the occupation, the manual labourers, agricultural labourers and house wives, drivers, construction workers and mill workers constituted 70% of HIV/TB cases in this region. This may be attributed to poor literacy, poverty, malnutrition, overcrowding, lack of knowledge of safe sexual practice, lack of knowledge of personal protection etc.

Analysis of the symptoms showed that all the cases were suffering from fever, the fever being low grade, intermittent in most cases. 96.6% cases had cough, 76.3% cases had weight loss, 37.3% cases had weakness and lassitude and 3.4% had hemoptysis. This correlated with the studies of Zuber Ahmad et al. [27] Purohit et al [28], Mohanty et al [29], and Gupta et al [30], fever was the most common complaint along with cough and anorexia and weight loss.

Sputum AFB was positive in 26 cases and was negative in 33 cases (44% and 56% respectively). This correlated with the study of E. J. Peters et al. [31] whose observation was 40%and 53% repectively. This supports

the findings of Sputum AFB positivity of 44 % by S. Rajasekaran et al. [32]

The radiological findings were infiltrations in 47% of cases, cavity in 22% of cases, consolidation in 14% of cases, pleural effusion in 12% of cases, hilar adenopathy in 3% of cases and military mottling in 2% of cases. It was observed that a total of 49 out of 59 cases (83%) presented as infiltrations, cavities or consolidation. This correlated with the studies of Soumya Swaminathan et al [33] and Zuber Ahmad et al. [34]

The WHO staging of the cases under study were that, in stage III there were 50 cases and in stage IV, there were 9 cases.

The CD4 counts in these cases studied were as follows. Among the 59 cases, 26 cases were sputum AFB positive and 33 cases were negative. Among the Sputum AFB positive cases, 16 cases had CD4 count less than 200; rest 10 cases were above 200. In the Sputum AFB negative cases, 19 were found to have CD4 count less than 200 and 10 cases above 200.

The correlation between the CD4 counts and the radiological manifestations were that at lower CD4 counts < 200 the pleural effusion and hilar adenopathy – 8 cases; consolidation 6 cases, cavity 3 cases and

infiltrations 20 cases. Whereas in cases with CD4 count >200, the findings were that 1 case of pleural effusion, 2 cases of consolidation, 8 cases of infiltrations and cavity seen in 10 cases.

In patients who have CD4 counts of 200 or more, chest X-Ray findings were upper lobe cavitation .In cases who have CD4 count fewer than 200/mm3, mediastinal adenopathy, miliary patterns , diffuse pulmonary infiltrations ,military mottling , absence of pulmonary cavitation and combined pulmonary and extrapulmonary disease are seen more often in patients with lower CD4 count. This observation correlated with the study by M. Hajiabdolbagi et al. [(35)], Pearlman DC et al [(36)], and Jones BE et al [(37)]

It was also observed that out of 59 HIV/PTB cases, 23 cases (15 male and 8 female cases) were on HAART already, which meant that these patients developed pulmonary tuberculosis during the period they were on treatment for HIV disease. Of these 23 cases 79% of cases (18 cases) were cavities and infiltrations. With correlation to the CD4 count, it was observed that there were 10 out of 11 cases of CD4 count less than 200 presenting as infiltrations and 4 out of 6 cases presented as cavities with CD4 count above 200. Post-HAART TB had the similar manifestations of tuberculosis occurring in advanced immune suppression. This is

supported by the previous Indian studies of Rajasekaran et al and S. Swaminathan et al. ([38, 39, and 40)] Higher Sputum smear negative pulmonary TB, higher proportion of extra-pulmonary TB and increased frequency of disseminated TB were observed in this study. The reason for the development of cavitatory lesions may be that in these cases immune reconstitution inflammatory syndrome (IRIS) may be responsible for the lesion. The reason for the development of PTB during HAART is that, HIV-induced depression of cellular immunity increases the susceptibility of individuals to develop tuberculosis through either reactivation of latent infection or rapid progression of a recent infection. The location and extent of tuberculosis in HIV-infected individuals depend largely on the degree of the immunosuppression, with an increased frequency of extrapulmonary and disseminated tuberculosis and lower field infiltrative pulmonary tuberculosis in the more severely immunocompromised.

Out of 23 cases only 8 cases were having a CD4 count of more than 200; rest was below 200. The likeliest explanation is that a proportion of HIV-infected patients, especially those with low nadir CD4 cell counts, have poor CD4 cell responses to HAART that may in some be related to lack of viral suppression. These patients are likely to retain a chronically heightened risk of TB. [(41, 42, 43.)]

Manifest - TB in HIV can also be a part of immune reconstitution inflammatory syndrome (IRIS). It is defined as transient worsening or appearance of new symptoms, signs or radiographic manifestations after initiation of highly active antiretroviral therapy (HAART). The incidence of IRIS in TB alone was 2%, with HIV co-infection was 7% and in those started on HAART was 36% as reported in a study by Narita et al [(44)]. The most common symptom of TB presenting as IRIS is fever along with worsening infiltrates on chest x-ray. Other manifestations include enlargement of the affected lymph nodes and liquefaction or appearance of new lymph nodes, pleural and pericardial effusion, ascites, central nervous system (CNS) lesions and visceral lesions. Risk factors for TB presenting as IRIS include early initiation of antiretroviral therapy (ART) within 2 months of starting antituberculous therapy (ATT), low CD4, presence of extrapulmonary TB especially of the CNS, disseminated TB and high viral load. The extent of immune reconstitution resulting from HAART is greatest during the first 2 years of treatment. Long-term HAART confers a greater reduction in TB risk than previously reported and HAART may, therefore, contribute more to TB control in low-income countries than previously estimated.

It was also observed that there were 8 HIV cases presently diagnosed as suffering from PTB; these patients were treated for tuberculosis earlier. These cases were started on CAT II ATT as per the RNTCP guidelines. To the surprise it was noted that out of 8 cases, 6 were cavities and infiltrations and out of the 6 cases 5 were sputum AFB positive.

These five cases can be, cases have an increased risk of developing drug resistance or MDR TB. The incidence of development of MDR TB in HIV patients is high compared to non HIV patients. The reasons may be a) poor absorption of the drug in the gut. b) Poor compliance to the drug either ATT or ART. c) Drug interactions of ARTdrugs with ATT drugs like, Rifampicin increases the cytochrome P 450 enzyme activity thereby causing decreased availability of PIs and NNRTIs [(45).] . The risk of drug resistance to ATT has not been proved in cases of HIV/TB cases. There are varying studies regarding this. In study conducted by C N Deivanayagam et al, it has been concluded that the amplifying and accelerating influence of HIV disease and delayed recognition of PTB among the HIV patients may contribute to the development of MDR TB among the HIV infected patients. [(46)] In a study by Akksilp S et al. it was found that HIV incidence was found to be high among the MDR TB patients, but not an independent risk factor for MDR TB. [(47)]

Hence apart from the diagnosis and management of HIV/TB cases, measures must be taken to identify the latent tuberculous infection at the earliest and treat.

ATT drug sensitivity test has to be carried out in all HIV PTB cases, to know the drug sensitivity pattern and to treat these patients effectively, in order to prevent MDR TB in HIV patients and also prevent the spread of the MDR TB in the community.

CONCLUSION

CONCLUSION

- Pulmonary Tuberculosis is one of the commonest opportunistic infection among the HIV positive individuals.
- The prevalence of Pulmonary tuberculosis is more in male than in female population of HIV positive individuals.
- Pulmonary Tuberculosis occurs early in the HIV infection even before the CD 4+ count falls to very low levels
- Manual labourers, agricultural labourers, etc of lower socioeconomic state with low literacy rate were more commonly affected by HIV-PTB co - infection.
- Fever, cough and loss of appetite and loss of weight were most common symptoms observed in HIV with Pulmonary TB co-infection/ individually.
- Sputum AFB was negative in tuberculosis presentations like hilar adenopathy, military mottling, pleural effusion etc.
- The radiological findings of infiltration were most common presentation, cavitatory lesions, consolidation, and pleural effusion etc follows. in that order. Lower the CD4 count, more were the incidence of pulmonary infiltration, pleural effusion, hilar adenopathy and military mottling. The cavitatory lesions manifest at higher CD4 counts.

- Sputum AFB negativity was more commonly seen in pulmonary tuberculosis of seropositive HIV individuals.
- Immune reconstitution inflammatory syndrome is seen in patients HAART wherein the latent TB or reinfection are seen.
- Treatment of TB can prolong the life and improve the quality of life for HIV-positive people.
- Knowledge of the clinico-radiological spectrum of tuberculosis and co-existing opportunistic infections is absolutely necessary for the early detection of the disease and initiating the treatment.
- As the rate of rise of PTB is increasing in the HIV endemic regions, improved diagnostic testing, especially directed towards early diagnosis of PTB and for the diagnosis of latent Tuberculous infection is the need of the day.
- The possibility of the occurrence of MDR TB has to be considered in cases in whom drug compliance is poor. These patients must be motivated with positive approach for regular treatment and must be monitored closely.
- Facilities for ATT drug susceptibility testing must be done at the time of diagnosis of PTB so that the ATT regimen can be modified accordingly.

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ANNEXURES

DEPARTMENT OF GENERAL MEDICINE, COIMBATORE MEDICAL COLLEGE .

STUDY OF CLINICO-DIAGNOSTIC PATTERN OF PULMONARY TUBERCULOSIS AMONG HIV PATIENTS

Informed consent form for prospective participants

Principal Investigator: Dr BALAJI. S, Junior Resident.

Research Guide: Prof. Dr. M. RAVEENDRAN, MD UNIT CHIEF, Medical Unit – IV.

Organization: Department of Medicine, Coimbatore Medical College Hospital.

This informed consent form has two parts

PART – I INFORMATION SHEET (to share the information about the research with you)

PART – II CERTIFICATE OF CONSENT (for signatures if you agree to take part)

(You will be given a copy of the full informed consent form.)

PART – I INFORMATION SHEET

I, Dr. S. BA.AJI, Junior resident in Dept of Medicine, invite you to join as participant in my research on manifestations of pulmonary tuberculosis in HIV patients, which is one of the serious infectious diseases in our country. I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.

Tuberculosis is the commonest opportunistic infection occurring among HIV positive persons in India and it is estimated that 60-70% of HIV positive persons will develop tuberculosis in their lifetime..
HIV infection has increased the burden of tuberculosis, especially in populations where HIV has become common, and where the prevalence of tuberculosis infection is high.
We are doing this research to learn the correlation of the CD 4 count and the manifestations of tuberculosis in the HIV positive patients and to acquire knowledge about the disease manifestations in our region so as to plan for early identification of the disease and better, management.

In this study you will have to answer questions regarding your illness, undergo a physical examination, give blood for tests, and undergo x ray examination and sputum examination.

You are being selected because we are inviting all HIV positive patients with chest symptoms suggestive of pulmonary tuberculosis attending our medical op, chest clinic/ HIV clinic to enroll in the study

Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. You may change your mind later and stop participating even if you agreed earlier.

You will have to give details regarding your age, duration of disease, family history of the disease, any symptoms you are having at present, your past medical problems, surgeries and current medications. A doctor will examine you to look for any problems. Your height and weight will be recorded. All the data will be recorded in a proforma. Ten ml of blood will be drawn for doing various laboratory tests to know about the status of your disease. Any excess sample will be destroyed immediately after the laboratory tests are completed. Taking the blood sample will produce some pain and there may be slight redness at the site of puncture for a day or two. . You will be subjected to X ray chest examination and you will give the sputum expectorated for examination. There will be no significant risk on exposure to X ray radiation and also no discomfort in collecting the sputum sample for examination.

On the first day you will be asked about your problems, a doctor will check you up. You will also have to give the blood. You will be taken the x ray chest and your sputum will be collected twice i.e. on two consequent days. You will be asked to collect the early morning sputum expectorated out after self inducing a cough.

In total you will have to visit twice or thrice for the research purpose. By participating in this research it is possible that you may experience some discomfort as each of your visits will take longer than your usual bi-weekly follow up visits and will involve needle pricks to give blood samples.

If you participate in this research you will be having a thorough check up, which may reveal some unidentified problems in you. We will promptly start the treatment for them. Also by participating you are providing valuable data that will help doctors understand this disease better and ultimately serve the patients in a better way.

We will not be providing any money for participating in this research; you may incur more expense since you will have to visit the hospital more frequently.

It is possible that if others in the community are aware that you are participating in this research, they may ask you questions. We will not be sharing the identity of those participating in the research with anyone. The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will not be identified by your name but by a number. Only the researchers will know what your number is and they will lock that information up with a lock and key. It will not be shared with or given to anyone except my research guide.

The knowledge that we get from doing this research will be shared with you before it is made widely available to the public. Confidential information will not be shared. There will be small meetings in the community and these will be announced. After these meetings, we will publish the results in order that other interested people may learn from our research

You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected.

If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact

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Unit Chief, Medical Unit –IV,
Dept of Medicine,
Coimbatore Medical College Hospital,
Coimbatore- 18.

This proposal has been reviewed and approved by the Ethics Committee of Coimbatore Medical College Hospital which is a committee whose task it is to make sure that research participants are protected from harm.

PART – II CERTIFICATE OF CONSENT

I have been invited to participate in research on pulmonary manifestations of HIV. I understand that it will involve answering a detailed questionnaire, undergoing a thorough physical exam, giving blood samples, taking X ray chest giving sputum samples for examination and two or three follow-up visits. I have been informed that the risks are minimal and may include only slight pain and redness at sight of needle prick. And no significant risk of exposure to X ray radiation or no discomfort in collecting the sputum samples. I am aware that there may be no benefit to me personally and that I will not be compensated monetarily. I have been provided with the name of a researcher who can be easily contacted using the number and address I was given for that person.

I have read the foregoing information or it has been read to me. I have had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research and understand that I have the right to withdraw from the research at anytime without in anyway affecting my medical care.

Name of the participant: _____

Signature of the participant: _____

Date: _____
(Day/Month/Year)

<u>If illiterate</u>

A literate witness must sign (if possible, this person should be selected by the participant and must have no connection to the research team)

I have witnessed the accurate reading of the consent form to the potential participant, translated to his mother tongue, and the individual has had opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness: _____ AND Thumb print of participant

Signature of witness: _____

Date: _____
(Day/Month/Year)

I have accurately read or witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of the researcher: _____

Signature of the researcher: _____

Date: _____
(Day/Month/Year)

PROFORMA

1. NAME AGE SEX
2. OCCUPATION MONTHLY INCOME
3. HEIGHT WEIGHT
4. ADDRESS

5. CLINICAL PROFILE
   FEVER COUGH HEMOPTYSIS
   LOSS OF WEIGHT LASSITUDE/ WEAKNESS
   H/O PRIOR ATT
6. SPUTUM AFB STATUS
7. CHEST X RAY FINDINGS
   INFILTRATIONS
   CAVITY
   CONSOLIDATION
   PLEURAL EFFUSION
   HILAR ADENOPATHY
   MILIARY MOTTLING
   OTHERS
8. BLOOD INVESTIGATIONS
   TC DC ESR
   HB%
   SUGAR UREA
   S.CREATININE
   LFT S. BILIRUBIN SGOT SGPT
   ALP
9. CD4 COUNT
10. ATT CATEGORY CAT I CAT II
11. DATE OF START OF A. ATT B. ART
12. OTHERS

MASTER CHART

S.NO	ART NO.	NAME	AGE	SEX	OCCUPATION	MONTHLY INCOME	SYMPTOMS					WEIGHT KG	INVESTIGATIONS										CHEST X RAY FINDINGS							SPUTUM AFB	CD4 COUNT	ON PRIOR ART	ATT CATEGORY	WHO STAGE
							FEVER	COUGH	HEMOPTYSIS	WEIGHT LOSS	LASSITUDE		HB%	TC	DC	ESR	S. BILIRUBIN	SGOT	SGPT	ALP	SUGAR	UREA	CREATININE	CAVITY	CONSOLIDATIC	INFILTRATIONS	MILIARY MOTT	PLEURAL EFFUS	HILAR ADENOP	OTHERS					
1	S 7482	MASILAMANI	40	F	LABOURER	1500	YES	YES		YES		37	9	7700	P64L36	26	0.4	33	30	87	84	33	0.9			RIGHT UZ					NEG	125	NO	I	III
2	S 6735	RAMU	35	M	LABOURER	2000	YES			YES		42	9.5	5400	P55L44	42	0.5	35	38	63	95	26	0.9					BILATERAL			NEG	67	NO	I	III
3	S 7309	MURUGESAN	47	M	CARPENTER	3000	YES	YES		YES	YES	40	9	7800	P60L40	18	0.8	42	36	38	100	30	0.8			RIGHT UZ					POS	104		I	III
4	S 4325	YUVARAJ	36	M	WORKSHOP	2500	YES			YES	YES	49	9.5	8800	P76L24	36	0.9	48	42	50	90	28	0.7					RIGHT			NEG	113	YES	I	III
5	S 7349	SRINIVASAN	45	M	LABOURER	4000	YES	YES		YES	YES	50	9.5	7600	P78L22	20	0.8	40	45	50	90	28	0.9			RIGHT UZ					NEG	385	NO	I	IV
6	S 7357	KUMAR	25	M	COKS WORKER	6000	YES	YES		YES		48	9.5	6200	P63L27	21	1.1	50	55	60	80	28	0.8		RIGHT UZ						POS	165	NO	I	III
7	S 2078	RAJENDRAN	38	M	MILL WORKER	4000	YES	YES		YES		50	10.5	7600	P58L38E4	18	0.9	40	45	60	84	26	0.8	LEFT UZ		BILATERAL UZ					POS	282	YES	I	IV
8	S 7452	GURUVAYURAPPAN	37	M	DRIVER	6000	YES	YES	YES	YES	YES	39	8.8	8600	P70L36E4	20	1.1	32	34	56	88	22	0.8	RIGHT UZ							POS	136	NO	I	III
9	S 4582	SENTHIL	37	M	VEG VENDOR	4000	YES	YES		YES	YES	43	10	5400	P55L44	26	0.9	26	23	77	115	30	0.9			BILATERAL UZ					NEG	96	YES	I	III
10	S1999	SAROJINI	48	F	HOUSE WIFE		YES	YES		YES		33	8.2	5400	P70L28E2	32	2.4	124	121	174	70	25	0.6			BILATERAL DIFFUSE					POS	644	YES	NON DOTS	III
11	S 4982	RAJKUMAR	30	M	MILL WORKER	4200	YES	YES		YES	YES	52	9.5	6200	P60L38E2	30	0.7	45	40	55	75	29	0.8				YES				POS	164	YES	I	IV
12	S 4928	RANI	40	F	AGRI LABOURER	3000	YES	YES				44	9	6600	P58L42	30	0.9	42	36	72	87	30	0.8	RIGHT UZ							POS	312	YES	II	III
13	S 7312	RANGASAMY	70	M	AGRI LABOURER	1500	YES	YES		YES		48	9.5	6800	P54L44E2	38	0.7	32	36	72	80	26	0.8	LEFT UZ							NEG	408	NO	I	IV
14	S 7342	MUMTAJ	42	F	HOUSE WIFE		YES	YES				35	11.2	6800	P70L36E4	30	1.1	30	32	60	80	30	1.1					LEFT			NEG	352	NO	I	III
15	S 7397	RUKMANI	38	F	AGRI LABOURER	2000	YES	YES		YES		40	10.2	5600	P60L40	22	0.8	30	32	70	90	28	0.9			RIGHT UZ AND MZ					POS	184	NO	I	III
16	S 5272	YUVAKRISHNAN	28	M	MILL SUPERVISOR	6000	YES	YES				58	11.6	6900	P78L22	36	1	36	34	70	72	26	1.1		RIGHT UZ						NEG	155	YES	I	III
17	S 7358	MARANNAN	29	M	DRIVER	6000	YES	YES		YES	YES	42	9	10000	P72L28	45	0.5	45	38	71	106	32	0.9		RIGHT UZ						POS	18	NO	I	IV
18	S 7401	KANNIYAMMAL	65	F	COKS WORKER	2000	YES	YES		YES		35	9	5800	P70L28E2	42	0.9	28	25	64	79	34	0.9								POS	112	NO	I	III
19	S 7333	PERUMAL	30	M	DHOBI	3500	YES	YES		YES		58	9	6800	P72L28	28	0.8	50	48	62	93	28	0.9			BILATERAL UZ					NEG	143	NO	I	IV
20	S 2560	VASUDARAU	41	M	LABOURER	1200	YES	YES		YES	YES	42	9.5	6700	P71L29	27	1.7	63	68	170	110	30	0.9	LEFT UZ							POS	51	YES	NON DOTS	III
21	S 7400	JOTHIMANI	35	F	AGRI LABOURER	1500	YES	YES		YES	YES	44	9.5	6400	P54L36	32	1	38	40	55	90	30	0.9		LEFT LZ						POS	31	NO	I	III
22	S 4866	JEYA	34	F	HOUSE WIFE		YES	YES		YES		42	9	7600	P55L45	30	0.7	30	36	62	88	20	0.8	RIGHT UZ							POS	216	YES	I	III
23	S 1180	LEELAVATHY	25	F	HOUSE WIFE		YES	YES				39	9.5	6700	P59L41	36	0.7	33	30	54	90	28	0.8			RIGHT UZ					NEG	84	NO	I	III
24	S 7499	GANESH	29	M	LABOURER	1000	YES	YES		YES		57	9.6	8700	P70L38E2	40	1	36	38	54	88	28	0.8	BILATERAL UZ							POS	584	NO	I	III
25	S 2302	KAVITHA	27	F	HOUSE WIFE		YES	YES		YES	YES	40	9.5	5900	P72L28	24	0.9	36	33	49	90	22	0.9			RIGHT UZ					NEG	209	NO	I	III
26	S 7493	INDHIRANI	35	F	MACHINE OPERATOR	2000	YES	YES				44	9.5	6200	P60L40	20	1	37	31	54	91	28	1						YES		NEG	159	NO	I	IV
27	S 7415	MURUGESAN	37	M	HIGHWAY LABOURER	1500	YES	YES		YES		39	12.4	6400	P74L26	25	1.4	56	58	166	92	24	0.9						YES		NEG	168	NO	NON DOTS	IV
28	S 2555	PALANISAMY	40	M	LABOURER	2200	YES	YES		YES	YES	47	9.6	8600	P54L40E6	38	0.9	32	28	85	80	32	1			RIGHT MZ					NEG	319	NO	I	III
29	S 7417	RANGARAU	54	M	COKS WORKER	1500	YES	YES		YES		47	9	6900	P62L38	23	0.8	35	32	56	96	27	0.8			LEFT UZ					NEG	259	NO	I	III
30	S 2520	GOPALASAMY	33	M	SECURITY PERSONNAL	2000	YES	YES				41	10	6800	P69L29E2	26	0.7	39	51	70	80	30	0.7	RIGHT UZ							POS	343	YES	II	III
31	S 7447	PUSHPALATHA	35	F	LABOURER	2000	YES	YES		YES		36	9.7	7200	P54L40E6	23	1.1	36	42	66	107	34	0.9					RIGHT			NEG	159	NO	I	III
32	S 5078	THANGAVEL	40	M	AGRI LABOURER	2000	YES	YES			YES	53	11	6800	P74L34E2	32	1.1	32	30	55	90	26	1			RIGHT UZ					NEG	184	YES	I	III
33	S 5586	SEKAR	41	M	DRIVER	3500	YES	YES		YES		38	10	5300	P70L38E2	28	0.4	33	30	72	110	25	0.8			RIGHT UZ				TB SPINE	POS	126	YES	II	IV
34	S 4715	LAKSHMI	4	FCH	STUDENT		YES	YES		YES		10	9.5	6800	P72L38	38	1.2	55	60	70	88	20	0.9		RIGHT MZ						NEG	359	NO	II	III
35	S 3120	KATHIRVEL	32	M	LABOURER	2000	YES	YES		YES		70	9.5	8800	P67L31E2	30	1.2	38	35	54	80	28	1.1			RIGHT UZ					NEG	234	NO	I	III
36	S 7474	NIKELAKUMAR	44	M	TRANSCRIPTIONIST	8000	YES	YES				70	12.5	8000	P70L30	20	1	34	38	68	102	34	0.9			RIGHT UZ					POS	61	NO	I	III
37	S 7572	MAHENDRAN	39	M	LABOURER	200	YES	YES	YES	YES		48	9.5	6200	P66L30E4	25	0.9	34	37	56	96	28	1	RIGHT UZ							POS	94	NO	I	III
38	S 7503	ANANDAKUMAR	37	M	TEMPLE PRIEST	1500	YES	YES		YES		52	11.6	8100	P78L22	18	0.8	33	20	48	80	30	1.1	LEFT UZ							POS	352	NO	I	III
39	S 5794	CHITRA	37	F	LABOURER	2000	YES	YES		YES		35	9.5	6900	P70L36E2	26	0.9	35	27	62	90	26	1	RIGHT UZ							POS	257	YES	II	III
40	S 3985	SENTHIL KUMAR	26	M	LABOURER	1000	YES	YES		YES		44	9.3	6100	P52L46E2	28	0.4	27	35	88	102	27	1			RIGHT UZ					NEG	37	NO	I	III
41	S 4678	NATARAJ	35	M	LABOURER	2000	YES	YES				45	10.2	7600	P69L31	28	1	33	35	56	90	22	1.1		RIGHT UZ						NEG	354	NO	I	III
42	S 6605	DHARMARAJ	40	M	LABOURER	2500	YES	YES		YES	YES	33	10	6400	P67L33	30	1.8	48	122	492	68	34	0.9			BILATERAL DIFFUSE					POS	117	NO	NON DOTS	III
43	S 7514	SUSEELA	47	F	HOUSE WIFE	2000	YES	YES		YES	YES	35	9.5	7900	P54L45	30	0.5	30	27	61	75	31	0.8			RIGHT UZ					NEG	48	NO	I	III
44	S 5860	ANDREW	38	M	COKS WORKER	6000	YES	YES		YES		47	10.8	7300	P64L36	32	0.8	32	33	66	80	40	0.8			RIGHT UZ					POS	167	YES	II	III
45	S 2788	RATHNAVEL	33	M	DRIVER	2500	YES	YES		YES	YES	56	9.5	6200	P58L42	28	0.5	34	30	68	108	35	1	LEFT UZ							NEG	72	NO	I	III
46	S 7546	CHITRA	48	F	HOUSE WIFE		YES	YES				35	9	7800	P56L44	38	1	33	40	69	92	22	0.8	RIGHT UZ	LEFT MZ,RIGHT LZ						POS	824	NO	I	III
47	S 6512	PARAVASIVAM	33	M	HOUSE WIFE		YES	YES		YES		40	9.8	6200	P59L40E1	28	0.9	30	32	50	80	28	0.8	LEFT UZ							POS	268	NO	I	III
48	S 1020	JOTHI	32	F	HOUSE WIFE		YES	YES		YES		45	10	5400	P68L32	20	1.4	32	37	69	88	25	1			BILATERAL UZ		RIGHT			NEG	180	YES	II	III
49	S 5421	SELVI	38	F	LABOURER	2000	YES	YES			YES	40	9.5	6200	P54L45	30	0.7	38	40	52	85	28	0.9			LEFT UZ					NEG	311	NO	I	III
50	S 3285	VASANTHA	30	F	LABOURER	2000	YES	YES		YES		48	9	5900	P59L40E1	22	0.5	32	30	55	143	32	0.6			BILATERAL DIFFUSE					NEG	23	YES	I	III
51	S 5818	THANGARAJ	54	M	SALESMAN	5000	YES	YES				62	9.8	7400	P78L22	34	1.7	40	42	165	90	32	0.8		LEFT LZ						NEG	267	NO	II	III
52	S 5592	KARUPATHAL	22	F	LABOURER	2000	YES	YES				48	9.2	6200	P55L45	22	0.8	32	34	62	80	20	0.8			RIGHT UZ					NEG	160	NO	I	III
53	S 5712	CHANDRAN	43	M	MASON	6000	YES	YES		YES	YES	50	10.2	6100	P58L42	28	1	36	58	198	85	30	1.1			RIGHT UZ					NEG	137	NO	NON DOTS	III
54	S 7582	MANICKAVASAGAM	37	M	BUSINESS	2000	YES	YES		YES	YES	46	9.8	6000	P70L30	22	0.8	22	30	60	80	20	0.9			RIGHT UZ					POS	94	NO	I	III
55	S 7581	MOHAMMAD SALI	35	M	COOK	4000	YES	YES		YES	YES	49	9.7	5900	P70L28E2	22	1.3	31	38	52	90	32	1			RIGHT UZ					NEG	209	NO	I	III
56	S 7578	CHINNU	45	M	BATTERY SHOP	2000	YES	YES		YES		60	9.8	6100	P74L26	26	0.9	30	32	50	86	28	1.1	RIGHT UZ							POS	185	NO	I	III
57	S 4300	ALI BADUSHA	32	M	MEDICAL SHOP	3000	YES	YES		YES	YES	47	10.8	5400	P75L25	30	0.6	23	19	71	70	28	1.1			RIGHT UZ					POS	97	YES	I	III
58	S 3713	PUSHPAM	35	F	LABOURER	2000	YES	YES		YES	YES	36	9.5	6300	P78L22	20	0.9	36	34	66	107	34	0.8					RIGHT			NEG	94	NO	I	III
59	S 7554	KALIMUTHU	34	M	PAPERMILL WORKER	3000	YES	YES			YES	60	9.2	6100	P76L24	26	0.8	29	35	78	80	28	0.9			RIGHT UZ					NEG	186	NO	I	III